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Review

Microparticle content of platelet concentrates is predicted by donor microparticles and is altered by production methods and stress

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ABSTRACT

In circulation, shedding of microparticles from a variety of viable cells can be triggered by pathological activation of inflammatory processes, by activation of coagulation or complement systems, or by physical stress. Elevated microparticle content (MPC) in donor blood might therefore indicate a clinical condition of the donor which, upon transfusion, might affect the recipient. In blood products, elevated MPC might also represent product stress. Surprisingly, the MPC in blood collected from normal blood donors is highly variable, which raises the question whether donor microparticles are present in-vivo and transfer into the final blood component, and how production methods and post-production processing might affect the MPC. We measured MPC using ThromboLUX in (a) platelet-rich plasma (PRP) of 54 apheresis donors and the corresponding apheresis products, (b) 651 apheresis and 646 pooled platelet concentrates (PCs) with plasma and 414 apheresis PCs in platelet additive solution (PAS), and (c) apheresis PCs before and after transportation, gamma irradiation, and pathogen inactivation (N = 8, 7, and 12 respectively). ThromboLUX-measured MPC in donor PRP and their corresponding apheresis PC samples were highly correlated ($r = 0.82$, $P = .001$). The average MPC in pooled PC was slightly lower than that in apheresis PC and substantially lower in apheresis PC stored with PAS rather than plasma. Mirasol Pathogen Reduction treatment significantly increased MPC with age. Thus, MPC measured in donor samples might be a useful predictor of product stability, especially if post-production processes are necessary.

Contents

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1. Introduction

Microparticles are an important factor in transfusion medicine [1–3]. These small vesicles found in blood plasma play complex and dynamic physiological roles as mediators of far-reaching intercellular communication by expressing a variety of membrane-associated proteins and by transferring receptors, growth factors, and microRNA [1–4]. Microparticles can be markers of inflammation [4] and hypercoagulation [3]. Microparticles are continuously released from red blood cells, white blood cells, endothelial cells, and platelets in response to epinephrine, ADP, thrombin, collagen, and Ca^{2+} ionophore, or as a result of the extracorporeal storage [1]. Seventy to ninety percent of microparticles are derived from platelets [5,6]. Platelets, in addition to responding to agonists, generate microparticles in response to complement activation, shear forces, senescence, and cytoskeletal abnormalities [2]. Increased concentration or altered characteristics of plasma microparticles in vivo are associated with hypertension [7], cardiovascular disease [8], recurrent miscarriage [9], transfusion-related acute lung injury [10], bacterial endotoxin [11], hypercoagulability in type 2 diabetes [12], Crohn's disease [13], sepsis [14,15], and auto-immune diseases such as rheumatoid arthritis, psoriasis and asthma [16–18], and melanoma [19]. In addition, the proportional increase of microparticle content (MPC) relative to platelet concentration during storage of platelet concentrate (PC) can be attributed to different methods of separation or varying processing conditions [20].

In blood products, elevated MPC might therefore indicate an undesirable condition in the donor that could affect the recipient after product transfusion. In fresh platelet products, MPC may indicate the level of stress that platelets were exposed to in the donor or during product separation [1,21]. Consequently, high MPC in the transfused platelet product could, for example, reduce platelet recovery by a direct effect on the recipient's immune system [1] or because the stress that generated the microparticles in the donor, or during product separation, marks the platelets for removal from circulation [22,23]. In addition, storage lesion also generates microparticles with aging of the platelet product [1,3]. Microparticles may participate in endothelial and macrophage activation, which in turn may shorten the platelet life span [24].

Surprisingly, the MPC in blood from normal healthy transfusion donors is highly variable and affected by diet [25,26] and exercise [27]. This observed variation raises the question of the extent to which donor microparticles transfer into the donated product and how production methods and post-production processing might affect the MPC. One immunocytochemistry study describes the carryover of donor microparticles into the apheresis product, where the microparticles appear to be mainly harvested from the donor [28]. Thus, MPC measured in donor samples might be a useful predictor of blood product MPC and therefore product stability.

Several technologies have been used and described in the literature for the measurement of microparticles in blood and other body fluids [1,21,24,29], including established methods such as flow cytometry and dynamic light scattering [30]. The measurement principle of the ThromboLUX microparticle assay is dynamic light scattering, which has long been used in the pharmaceutical industry for quality control of liposomal drugs, which are in the size range of microparticles. Dynamic light scattering is ideally suited for routine screening of particle content based on size but not for functional characterization of these particles. The special DLS setup in ThromboLUX also allows microparticle enumeration to be performed in native platelet-rich plasma and platelet concentrate samples, i.e., without removal of platelets, which is essential for routine screening. The ThromboLUX microparticle assay is validated as a measure of MPC in pooled PC because it correlates highly with measures of microparticle concentration obtained by flow cytometry [31].

We hypothesized that the origin of microparticles in PCs is the donor, and that post-production processing – such as substitution of plasma with platelet additive solution (PAS), transport, irradiation, or pathogen inactivation – can decrease or increase the MPC. Accordingly, we investigated the relationship between the MPC of each donor's platelet-rich plasma (PRP) sample before apheresis and the MPC in the donor's corresponding apheresis PC. We chose apheresis

product rather than pooled PC in order to obtain a one-to-one comparison for each donor. In addition, to compare MPC in different types of platelet products and post-production conditions, we analyzed data sets obtained from two large clinical studies and performed stress tests. To first validate the ThromboLUX microparticle assay for apheresis PC, we performed an inter-device comparison with flow-cytometry.

2. Materials and methods

2.1. ThromboLUX-measured microparticle content

Analysis of dynamic light scattering and calculation of the ThromboLUX score have been described elsewhere [30]. ThromboLUX (LightIntegra Technology Inc., Vancouver, BC, Canada) measures the microparticle contribution to the total scattering intensity in the sample. The relative contributions of microparticles, platelets, and microaggregates to the dynamic-light-scattering signal were determined and particle size histograms were obtained. Microparticle content was shown in the particle size distribution as particles with radii between 50 nm and 550 nm (Fig. 1A). Microparticle content reflects the relative contribution or proportion of microparticles compared to platelets and is therefore also a function of the platelet concentration of the sample.

Accordingly, the absolute microparticle concentration is calculated by multiplying the ThromboLUX-reported microparticle factor by the platelet count obtained with a hematology analyzer. Exosome-sized particles with radii below 50 nm are also shown in the size distribution (Fig. 1A)

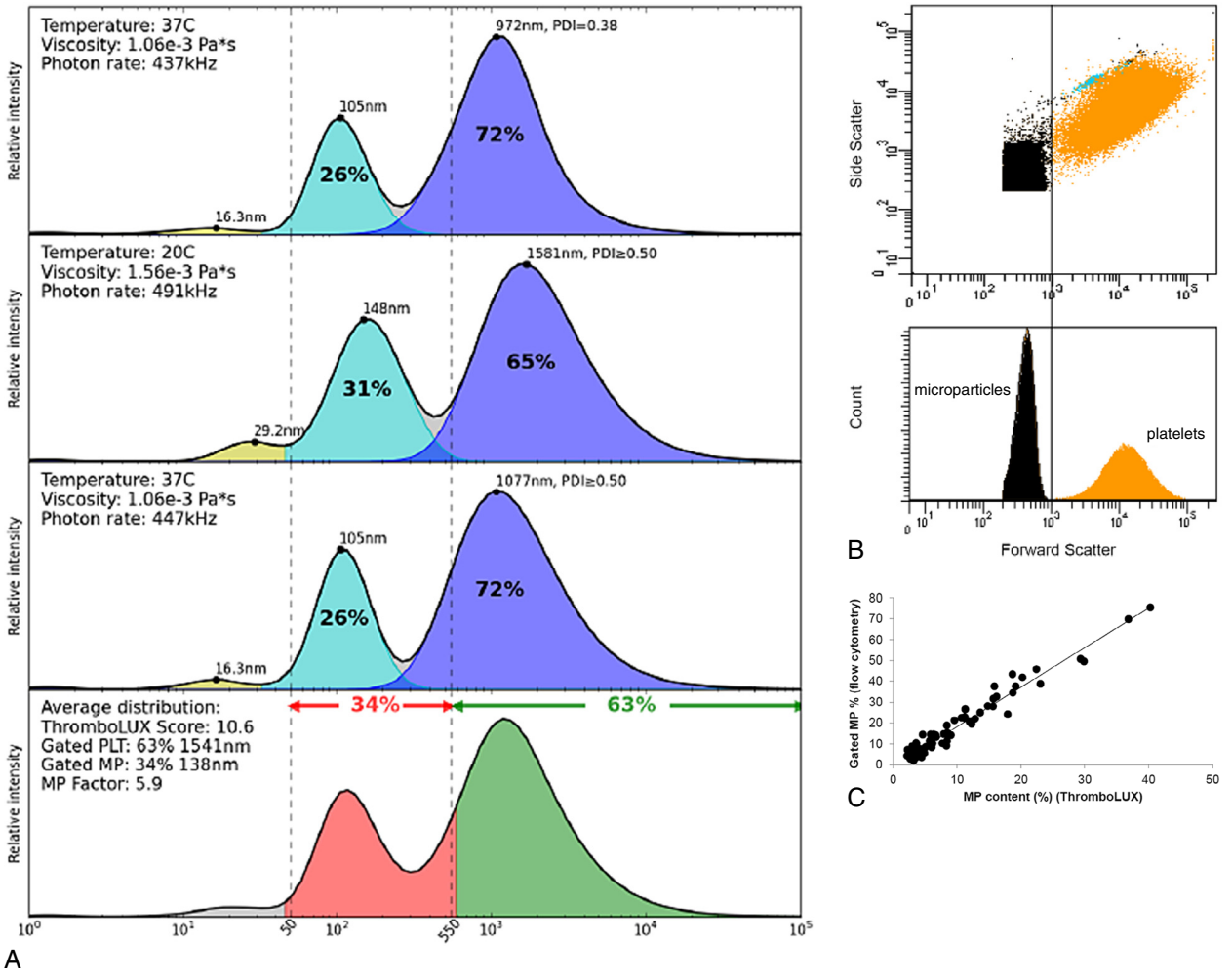

Fig. 1. Comparison of MPC in apheresis PC determined by ThromboLUX and flow cytometry. (A) Example of ThromboLUX test results showing the contribution of exosome-sized particles (radii below 50 nm), microparticles (radii 50–550 nm), platelets, and microaggregates (radii above 550 nm). The ThromboLUX test consists of 3 sequential intensity measurements at 37 °C, 20 °C, and 37 °C. Scores are calculated for each measurement and averaged for the final score. (B) Example obtained with flow cytometry of a scatter plot and histogram showing platelet and microparticle events. (C) Scatter plot showing high correlation with flow cytometry ($r = 0.98$, $P < .0001$, N = 71 samples). PLT, platelet; %, percent of area under the relative-intensity curve; MP, microparticle; PDI, polydispersity index; gated MP %, gating by size.

2.2. Flow cytometry

Standard flow cytometers have manufacturer-recommended detection limits within the microparticle size range of about 500 nm–1 μm. However, with certain instrument and parameter settings, the use of internal-calibration flow cytometry has been shown to adequately measure microparticles [31–33]. For internal calibration, fluorescently labeled polystyrene beads are added. Ten thousand fluorescently-labeled 1-μm polystyrene beads are counted as fluorescence events, providing normalization of the platelet and microparticle counts, which are gated separately by their forward and side scatter. The percentage of microparticles in a sample is calculated as the number of gated microparticle events divided by the total number of non-fluorescent events (Fig. 1B).

Flow cytometry was performed on a FACSCanto II flow cytometer with FACSDiva software version 6.1.3 (BD Biosciences, Becton, Dickinson and Company, San Jose, CA, USA). Reagent solution of 0.2% formaldehyde in normal saline was prepared by dissolving 9.00 g of sodium chloride in 1000 ml of distilled water, then adding 5.4 ml of 37% formaldehyde stock, mixing, and storing in a closed container at room temperature. Microspheres (Flouresbrite Carboxylate YG 1.0-μm yellow-green, Polysciences Inc., Warrington, PA, USA) were diluted 1 in 200 in distilled water (Gibco Life Technologies Inc., Burlington, ON, Canada). The PC was sampled in a laminar flow cabinet using aseptic technique. Flow cytometry settings were as follows. FSC-H: 700 V, SSC-H: 400 V, FL1 PMT: 320 V, threshold (FSC and SSC): 200, flow rate: low, bi-exponential display: ON.

2.3. Sample preparation

All blood products were collected with informed consent from healthy volunteer donors under an institutionally approved human use protocol. Collection, processing, and storage followed United States Food and Drug Administration (FDA) and American Association of Blood Banks (AABB) guidelines.

To compare MPC measured with ThromboLUX and flow cytometry, 40 apheresis PCs (Trima Accel, Terumo BCT, Lakewood, CO, USA) were collected over a period of 10 weeks and tested on day 1 of storage. Thirty one of these PCs were also tested on day 5 of storage (N = 71).

Donor PRP was obtained from 54 apheresis donors to evaluate ThromboLUX for donor testing before the production of apheresis concentrates. Fresh EDTA anticoagulated whole blood samples were obtained. PRP was obtained by centrifuging at 150 *g* (depending on the centrifuge and rotor this might be 800–1100 rev min^{-1}) for 12 minutes at 22–24 °C. The supernatant PRP was collected with a plastic transfer pipette into a microcentrifuge tube or equivalent container and kept on the mixer. The capillary was filled with 100 μl of the sample following the ThromboLUX Test Kit instructions for use. PRP was analyzed on the ThromboLUX according to the Operator's Manual. Each sample was tested in duplicate. The corresponding donor apheresis PCs were obtained using a Trima Accel (Terumo BCT, Lakewood, CO, USA).

To compare different types of platelet products, the MPC of 1711 platelet products was measured over the course of two large clinical studies conducted in hospitals in Vancouver (961 samples) and New York (750 samples). In Vancouver, a large ThromboLUX data set from apheresis PC (Trima Accel, Terumo BCT, Lakewood, CO, USA) and buffy-coat pooled PC (platelets from four whole blood donors pooled with the plasma of one of the four donors) was gathered at the Vancouver General Hospital in 2010–2014. Samples were obtained aseptically from PC before they were transfused to hematology–oncology patients.

In New York, MPC in apheresis PC with either plasma or PAS as suspension media was determined before transfusion to oncology patients. A large data set was collected from apheresis PC sampled prior to being sent from the blood bank at North Shore University Hospital, 300 Community Drive, Manhasset, NY 11030 to the Monter Center for transfusion. At the blood bank it is routine practice to retain a sample, in an FDA-cleared Fenwal blood storage pack (20 ml PVC plastic), from any platelet component immediately prior to transfusion for availability for bacterial screening in the event that a transfusion reaction is reported. Within 4 hours of collection ThromboLUX testing was performed on a surplus specimen of that sample at the Feinstein Institute for Medical Research. The volume ratio of PAS and residual plasma was 65:35. Machines used for apheresis collection were the Amicus (Fenwal, Lake Zurich, IL, USA) for PAS concentrates and the Trima Accel (Terumo BCT, Lakewood, CO, USA) for plasma concentrates. The mean microparticle concentration for platelet products was individually calculated using the measured platelet counts (Sysmex XD 2100, Lincolnshire, IL, USA).

To test the effect of exposure to the stressors of gamma irradiation and transport, samples were obtained from tubing on the bag of the platelet apheresis concentrate (MCS+, Haemonetics, Munich, Germany) after the tubing was stripped three times with a manual stripping device. The entire concentrate was agitated gently between each stripping step to mix the content. Segments were removed from the tubing by heat sealing and cutting an approximately 5-cm long piece. The top of the segment was cut open to access the sample for aspiration into the ThromboLUX capillary. Fifteen test samples of apheresis PCs were obtained from 15 unique volunteer apheresis donors.

Samples were tested with ThromboLUX before and after gamma irradiation with an IBL 437C irradiation device using a Cesium-137 source and a center target dose of 25 Gy (Gamma-Service Medical GmbH, Leipzig, Germany) on day one after production (time difference of 4–8 hours, N = 8), as well as before and after simulated transport (N = 7).

To test for the effect of exposure to the stressor of pathogen inactivation, apheresis platelet concentrates were obtained from deferred normal volunteer donors at the Canadian Blood Services netCAD Research Donor Clinic. The study protocol met the standards of the Declaration of Helsinki and was approved by the Canadian Blood Services ethics review committee. In accordance with the Declaration of Helsinki, informed consent was obtained from all donors. Apheresis platelet concentrates were prepared using the Trima Accel (Terumo BCT, Lakewood, CO, USA) auto-

mated blood collection system. Twelve double platelet samples were collected, rested for a minimum of 2 h, then divided into 2 equal components by weight. One component was treated by the Mirasol Pathogen Reduction Technology System (Terumo BCT, Lakewood, CO, USA): transfer to a Mirasol storage bag, addition of 35 ml of riboflavin solution, and exposure to a metered dose of UV light in the Mirasol illuminator. The control component was transferred to a Mirasol storage bag and received 35 ml of a 0.9% saline solution, the same carrier solution that dissolves the riboflavin, to ensure that both components had the same platelet concentration. Components were sampled and tested on days 1, 2, 5, and 7 post-collection.

2.4. Data analysis

Data analysis was aimed at determining the distribution of microparticles in PCs and the difference between apheresis and pooled PCs in their relative and absolute MPCs. All statistical analysis was performed using Microsoft Excel 2013 and Minitab version 17.2.1. Pearson's correlation coefficients were calculated for bivariate regressions between MPC in donor PRP and MPC in samples of corresponding apheresis PC. Two-sample t-tests were performed for the comparison of different types of platelet products. A P value of <.05 was considered statistically significant.

3. Results

3.1. Inter-device comparison of apheresis MPC measured by ThromboLUX and flow cytometry

ThromoLUX-measured MPC was highly correlated with MPC enumerated by flow cytometry in the same samples of apheresis PCs (Fig. 1C; $r = 0.98$, $P < .0001$). Moreover, the ratio of microparticles to intact platelets as measured by the two devices was also very similar.

3.2. Prediction of apheresis product MPC by the MPC of the donor's PRP

Microparticle content in donor PRP samples was not normally distributed across donors (Fig. 2.). The apheresis process, which enriches platelets, decreased the MPC in the apheresis platelet product by an average of 75% (Fig. 3). In this study, only 2% of apheresis products contained more than 30% microparticles (Fig. 3).

Levels of microparticles in apheresis-donor PRP samples were highly correlated with levels of microparticles in the corresponding apheresis platelet donation immediately after PC collection (Fig. 4). When donor MPC was high, MPC in the corresponding apheresis PC tended to be high as well (Fig. 5). In addition, the higher platelet count in the PC necessitates a proportionately lower relative MPC value in the product of approximately 34% of the MPC in the donor PRP. Accordingly, a linear model describes the relationship of MPC in donor and product samples of this data set with the following equation:

$$Product\ MP = -0.01106 + 0.3388 \times Donor\ MP$$

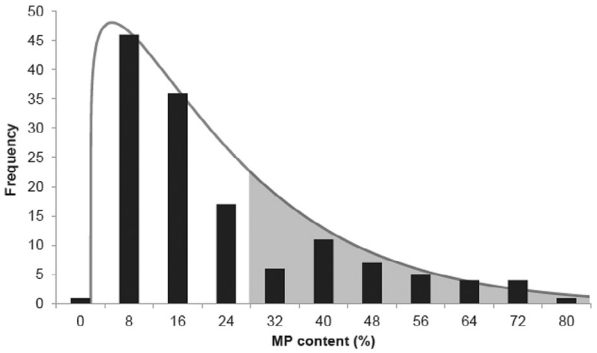

Fig. 2. Histogram of MPC in donor PRP (bars) compared to best fit 3-Parameter Weibull distribution (gray curve), showing that 33% of 54 donor PRP samples contained more than 30% microparticles (gray shaded area). The probability plot for MPC (N = 53) showed a mean of 20.6% and very wide distribution with 5 and 95 percentiles of 4.4% and 68.2%.

3.3. Estimate of microparticle concentration from large trial data sets

3.3.1. Vancouver General Hospital

The best fit of the histogram data for the distribution of microparticle concentration (particles ranging in radii from 50 to 550 nm) was obtained with a 3-parameter lognormal distribution curve for both apheresis PCs and pooled PCs. The mean microparticle concentrations in apheresis PC in plasma and in pooled PC in plasma were 3.7×10^{12} l^{-1} [15.6 ± 11 (SD)%, 315 samples, 95% CI = 14–17%] and 3.2×10^{12} l^{-1} [21.1 ± 13 (SD)%, 646 samples, 95% CI = 20–22%], respectively. These differences were significant ($P < .05$).

The average platelet count for apheresis concentrates was 1.476×10^{12} platelets l^{-1} and for pooled PCs was 9.27×10^{11} platelets l^{-1}. Thus, the mean MPC, which was proportional to platelets, was significantly higher (5.6%, $P < .001$) in pooled

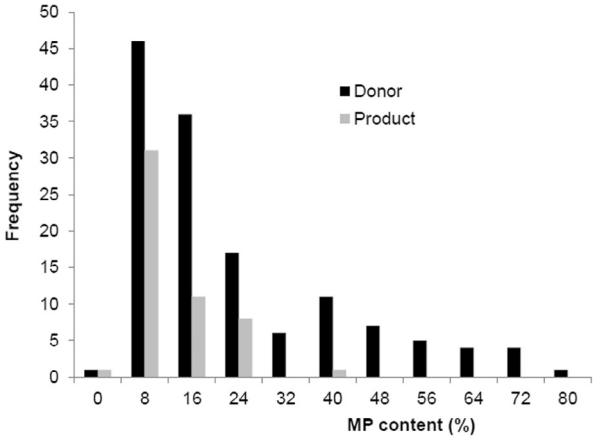

Fig. 3. Histograms of MPC in 54 donor PRP (light bars) and the corresponding apheresis PCs (overlapping dark bars). This data set for both PRP and apheresis PC was best approximated by a Weibull distribution because most donors had a very low MPC. Enrichment of platelets in the apheresis product is shown by the mean (50th percentile) MPC, which is 20.6% for donor samples and only 5.1% for the corresponding product. MP, microparticle.

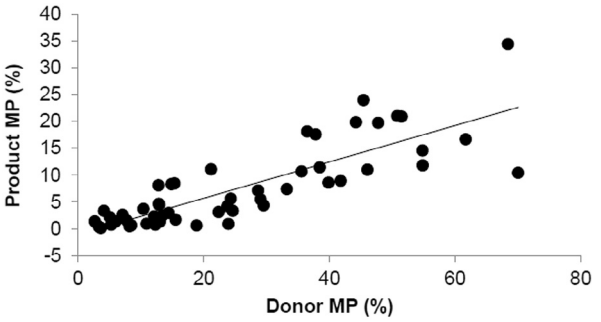

Fig. 4. Regression scatter plot for MPC for all particles with radii in the range of 50–550 nm in 54 donor PRP compared to samples from the corresponding apheresis product; $r = 0.82$, $P = .001$. MP, microparticle.

than apheresis concentrates. However, when taking the much lower platelet count of pooled concentrates into account, the mean microparticle concentration was lower in pooled products compared to apheresis products.

The size distributions also showed that 62 of 315 (20%) apheresis and 364 of 646 (56%) of pooled concentrates contained detectable numbers of particles with radii below 50 nm. In addition, a higher content of these small particles (3–5% relative intensity detected with ThromboLUX) was found only in pooled concentrates (n = 19). The mean radius ± standard deviation for these populations was 7 ± 3 nm in both apheresis and pooled PCs.

3.3.2. New York

Table 1 compares MPC and microparticle concentration (for samples with known platelet count) in apheresis PCs with either plasma (n = 336 or 98) or PAS (n = 414 or 133) as the suspension medium. The best fit of the histogram data for the distribution of MPC in samples with plasma as the medium was obtained with a 2-parameter exponential distribution curve as a probability plot. The probability plot for MPC showed a mean of 8.6% and a very wide distribution (5 and 95 percentiles of 1.1% and 35.3%) reflecting the variability of MPC in plasma-containing PC. In contrast, the best fit for MPC from PCs with PAS as the medium was obtained with a lognormal distribution curve. Here the probability plot for MPC showed a mean of 6.1% with a narrower distribution (5 and 95 percentiles of 1.3% and 28.3%) indicative of lower variability of MPC in PAS-containing PC. The mean microparticle concentration and distribution of microparticles in PAS were substantially lower than those in plasma products (MPC only reduced to 78%, MP concentration reduced to 42%, Table 1.

Particles with radii below 50 nm were detected in 264 of 336 (79%) of plasma-containing PC and 49 of 414 (12%)

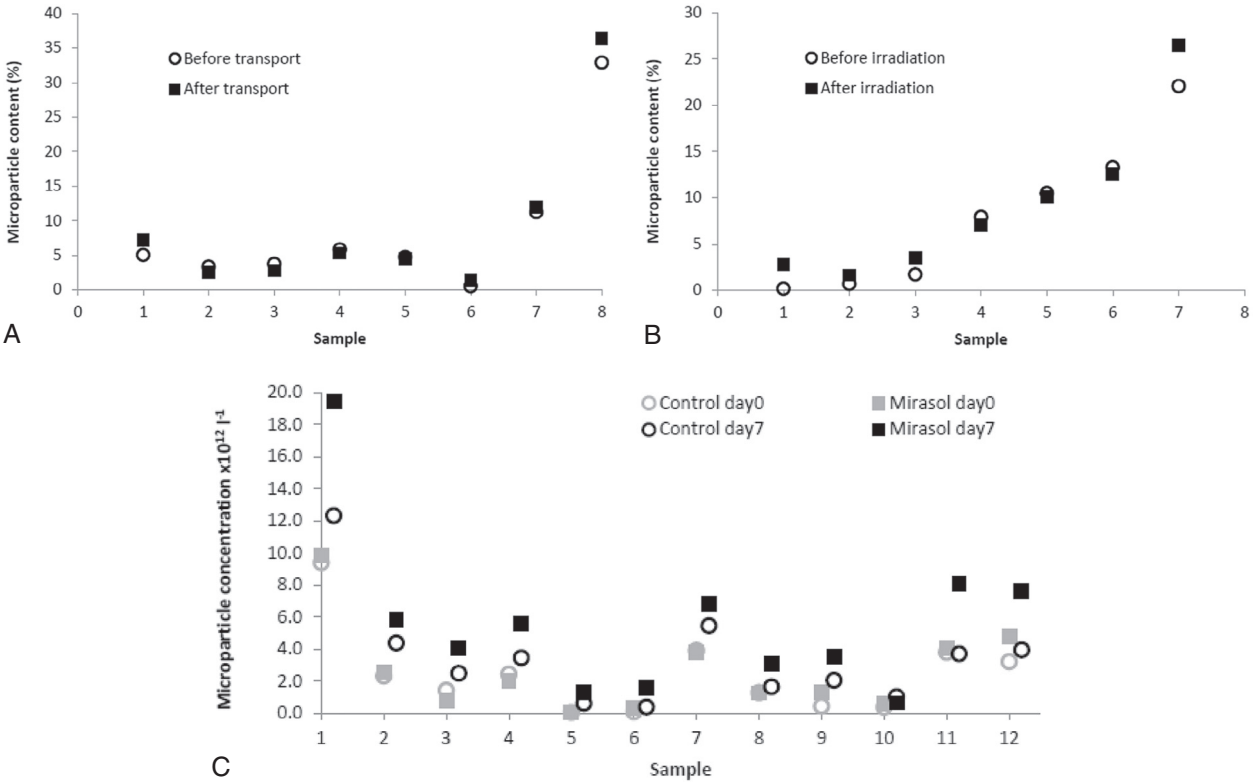

Fig. 5. Effect of post-production processes on MPC of platelet concentrates. Means of MPC in apheresis concentrates with plasma did not change significantly with transport in 8 samples (A), gamma irradiation in 7 samples (B), or pathogen inactivation with Mirasol in 12 samples compared to control on the day of production (C, gray symbols are day 0). On day 7 of storage the means of MP concentrations in control and Mirasol-treated concentrates (C) were very significantly different (control $3.5 \pm 3.2 \times 10^{12}$ l^{-1}, Mirasol-treated $5.6 \pm 5.0 \times 10^{12}$ l^{-1}, $P = .003$).

Table 1
Comparison of relative MPC and microparticle concentration (calculated for product with known platelet count) in apheresis PCs with plasma or PAS suspension medium tested in New York.

	Plasma MPC %	PAS MPC %	Plasma microparticle $\times 10^{12}$ l^{-1}	PAS microparticle $\times 10^{12}$ l^{-1}
Sample size	336	414	98	133
Mean MPC	12.1	9.5	3.3	1.4
95% CI[a]	10.8–13.4	8.5–10.6	2.6–3.9	1.2–1.6
Standard deviation[a]	8	11	3.2	1.3
Difference between means[a]	2.6 ($P = .002$)		1.9 ($P < .0001$)	

[a] Assuming a normal distribution of data.

of PAS-containing PC with average contributions to the ThromboLUX-measured relative intensity of only 1%. The mean radii ± standard deviations for these populations were 11.3 ± 5 nm for plasma and 15.6 ± 5 nm for PAS products, respectively.

3.4. Effect of post-production stressors on microparticle content

3.4.1. Gamma irradiation and transport

No significant effect was found in these small samples (7 and 8, respectively).

3.4.2. Mirasol pathogen reduction

The difference between means for microparticle concentration in apheresis PCs with or without Mirasol treatment was highly significant ($P = .003$) on days 5 and 7 compared to controls. On day 7 the mean increase in MP concentration in the Mirasol arm was 2.2×10^{12} l^{-1} (95% CI = 0.9–3.4 $\times 10^{12}$ l^{-1}). The changes were correlated with the level of initial concentration.

4. Discussion

Our results indicate that the origin of microparticles in apheresis PCs immediately after separation is the donor, and that the type of product, the suspension medium, and post-production pathogen-inactivation alter the MPC. Evidence for the donor origin of microparticles is that the MPC of donor PRP samples before apheresis was highly correlated with the MPC in the donor's corresponding apheresis PC.

Evidence for product and post-production differences is (a) the platelet concentrate MPC data sets from two large clinical trials showing that the mean microparticle concentration was lower in pooled products compared to apheresis product, (b) the finding that mean microparticle concentration in PAS was substantially lower than that in plasma products, and (c) the finding that Mirasol treatment in combination with 5 or more days of storage increased MPC.

Because apheresis concentrates in PAS have only 35% plasma left, it was expected that PAS products would contain much fewer microparticles than plasma products, as we have found. Surprisingly, despite the removal of microparticles with 65% of the plasma and replacement of that volume with microparticle-free PAS, the PCs with PAS showed an MPC – the ratio of microparticles to platelets – that was similar to PCs with plasma. This unexpectedly high percentage of MPC was caused by the loss of platelets, which was unexpected. For the calculation of the actual concentration, the true platelet count was used and therefore showed a much lower concentration, as expected. It follows that our findings might explain the lower frequency of adverse reactions in recipients of PAS compared to plasma product [34] because of the substantially lower content in microparticles, which have been reported to be inflammatory markers.

ThromboLUX-generated data contain information on the content of smaller, exosome-sized particles with radii below 50 nm. These are very different particle populations than microparticles and could comprise proteins or protein aggregates as well as exosomes which are derived from different cellular pathways, probably containing different cargoes and having different effects than microparticles. Further research is warranted to determine why the heterogeneity of these small particles was greater in pooled compared to apheresis products in Vancouver and what the source of the mean size and overall concentration differences seen between Vancouver and New York might be.

Although our pilot study of stressors on apheresis PC from 7 to 8 donors showed no effect on MPC by simulated transportation or gamma irradiation, more extensive studies on post-production processing effects on MPC are recommended.

Further evidence that MPC in transfusion-product recipients can limit the effectiveness of platelet transfusion in a clinically important way has been found in a recent study by our group (unpublished results). In this study, ThromboLUX-measured microparticle content was inversely correlated with recovery of radiolabeled fresh donor platelets after reinfusion ($r = –0.50$, $P = .001$). In addition, other studies suggest that high MPC has a negative effect on transfusion outcome of prophylactic transfusions [21,24]. However, the pro-coagulant activity of microparticles might be beneficial in therapeutic applications to stop heavy bleeding. Thus, screening platelet concentrates for high and low MPCs may be helpful for targeted use of donor-to-patient matched platelet concentrates depending on the application.

A question that arises is whether donor MPC is stable over time in apheresis donors who donate regularly. Considering that microparticles were described as markers of inflammation [4], donors might be stable with high MPC due to chronic conditions (for example with asthma, allergies, or high interleukins) or might not be stable (for example, a window period of infection, or other transient condition). During the study reported here, some donors were tested up to 3 times, and we found that some changed and some did not. An interesting future study would be to collect additional information from the donor to find out why they have "chronic" or "transient" high MPC.

Monitoring the MPC content of blood products could allow interventions such as nanoparticle filtering. Filtering of plasma with a nanofilter of 75 nm greatly reduces MPC and decreases thrombin generation in vitro without affecting the protein content or the activity of coagulation factors [29]. Nanofiltering might therefore make it possible to remove microparticles from plasma that is returned to the donor during apheresis collection to benefit the donor as well as the PC recipient.

Flow cytometry faces limitations with regard to detection limits for small size and the standardization of methods, which are not relevant to the ThromboLUX assay [35–38]. Furthermore, flow cytometry is not suitable for routine quantitation of microparticles in PCs because this technique requires sophisticated and expensive instrumentation, highly trained personnel to perform the test and interpret the results, and several steps of sample preparation. In contrast, ThromboLUX does not require sample preparation and determines microparticle content automatically. However, flow cytometry, which is based on the detection of specific binding of fluorescently labeled antibodies, can be used to identify the cellular origin and potential function of microparticles. In this light, ThromboLUX and flow cytometry could be viewed as companion technologies where the ThromboLUX assay is performed to quickly screen samples for MPC and then flow cytometry is used to subsequently characterize the microparticles when the detected amount warrants further investigation.

In conclusion, knowing that MPC in the donor carries over into the corresponding product and is altered during and after production allows us to identify platelet products that may be less viable or less resistant to post-production stress.

Therefore the ThromboLUX microparticle assay, validated as a measure of MPC in both apheresis and pooled PC, could reduce the risk of ineffective transfusions.

Consequently, the complications associated with ineffective transfusions would be reduced. In the long-term, characterizing MPC in platelet products to gain improved clinical effectiveness could dramatically lower the cost of platelet transfusion therapy for hospitals and healthcare systems.

Authors' contributions

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